US010934241B2

(12) **United States Patent**
Laali

(10) **Patent No.: US 10,934,241 B2**
(45) **Date of Patent: Mar. 2, 2021**

(54) **CURCUMINOID-INSPIRED SYNTHETIC COMPOUNDS AS ANTI-TUMOR AGENTS**

(71) Applicant: **Kenneth K. Laali**, Jacksonville, FL (US)

(72) Inventor: **Kenneth K. Laali**, Jacksonville, FL (US)

(73) Assignee: **University of North Florida Board of Trustees**, Jacksonville, FL (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **16/010,822**

(22) Filed: **Jun. 18, 2018**

(65) **Prior Publication Data**

US 2018/0362433 A1 Dec. 20, 2018

Related U.S. Application Data

(60) Provisional application No. 62/520,788, filed on Jun. 16, 2017.

(51) **Int. Cl.**

C07C 49/235	(2006.01)
C07C 49/255	(2006.01)
C07F 5/02	(2006.01)

(52) **U.S. Cl.**

CPC ***C07C 49/255*** (2013.01); ***C07C 49/235*** (2013.01); ***C07F 5/022*** (2013.01)

(58) **Field of Classification Search**

CPC C07C 49/255; C07C 49/235; C07F 5/022

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

1,009,550	A *	11/1911	Moys	B67D 7/163 141/381
7,355,081	B2 *	4/2008	Lee	C07C 49/248 568/36
9,375,408	B2 *	6/2016	Singh	A61K 31/12

OTHER PUBLICATIONS

Gupta, Subash C. et al. Multitargeting by curcumin as revealed by molecular interaction studies. Nat Prod Rep. Nov. 2011; 28(12): 1937-1955.

(Continued)

Primary Examiner — Savitha M Rao
Assistant Examiner — Andrew P Lee
(74) *Attorney, Agent, or Firm* — Smith & Hopen, P.A.; Michele L. Lawson

(57) **ABSTRACT**

Novel CUR— and CUR—BF_2 compounds exhibiting anti-tumor properties are presented. CUR compounds bearing fluorinated moieties with selective fluorine introduction into the α-carbonyl moiety as well as CUR—BF_2 adducts and CURs with diverse substitution patterns in the phenyl rings including fluorinated substituents (SCF_3, OCF_3, and F) and/or bulky activating groups (OMe, OAc, and OBz) are presented. Fluorinated aryl-pyrazoles and isoxazoles as well as novel CUR and CUR—BF_2 compounds with monocyclic aromatic and bicyclic-heteroaromatic lateral rings, bearing fluorine(s), OCF3, CF3, and SCF3 groups, and their alpha-carbonyl-fluorinated analogs, as well as their pyrazole and isoxazole derivatives are presented. The CUR-pyrazoles embody analogs that are fluorinated at the phenyl-pyrazole moiety. The compounds and their derivatives exhibited exceptional cytotoxic and anti-proliferative activity against several cancer cell-lines. Deuterated CUR—BF2 and CUR compounds were also synthesized.

7 Claims, 97 Drawing Sheets